

AMENDMENTS TO THE SPECIFICATION:

Please replace the Abstract of the Disclosure with the following rewritten Abstract which appears as an appendix.

On page 1, after line 3, please add the following heading:

--BACKGROUND OF THE INVENTION--

--Field of the Invention--

On page 1, after line 7, please add the following heading:

--Description of the Related Art--

On page 1, please delete lines 8-29 through page 2, lines 1-20.

On page 3, after line 12, please add the following heading:

--SUMMARY OF THE INVENTION--

Please replace the paragraph beginning at page 3, lines 13-20 (second full paragraph) with the following rewritten paragraph:

--The present invention aims to propose a method and apparatus for fibred high-resolution fluorescence imaging, in particular confocal imaging, of the type using an image guide

made of optical fibres scanned one by one by an excitation beam emitted continuously, said method and apparatus making it possible to obtain the display in real time of a site ~~in vivo in situ~~ in vivo and in situ, i.e. capable of providing a sufficient number of point by point images per second without being dependent on the movements of the subject and the operator in order to obtain in particular a fairly rapid examination.--

Please replace the paragraph beginning at page 3, lines 24-31 through page 4, lines 1-5, with the following rewritten paragraph:

--According to a first feature of the invention, a method is proposed for the realization of a confocal fluorescence ~~in vivo in situ~~ in vivo and in situ image, the method using an image guide made of several thousands of optical fibres and consisting of the point by point scanning of a tissue in a subsurface plane, each point corresponding to an excitation signal emitted by a continuous source, deflected and injected into one of the optical fibres of said bundle then focused on the exit of said fibre in said plane, each point emitting in return a fluorescence signal collected by said optical fibre, then detected and digitized to form an image element, characterized in that the excitation signal is deflected at a speed corresponding to acquisition of a number of images per second sufficient for a real-time use and in that the fluorescence signal is detected at

a detection, frequency corresponding to a minimum sampling frequency of the fibres one-by-one.--

On page 4, after line 6, please begin new paragraph and add the following:

--The fluorescence observed may come from an exogenous compound (typically an injected marker) or an endogenous compound (present in the cell) of a biological tissue.

More particularly, the method of confocal imaging according to the invention is of the type which consists of scanning a tissue point by point in a subsurface plane, each point corresponding to an excitation signal emitted by a continuous source, deflected and injected by turns into an optical fibre of a bundle of optical fibres, then focussed at the exit of said fibre in said plane, each point emitting in return a fluorescence signal collected by said optical fibre, then detected and digitized to form an image element.

The confocal character is obtained using the same optical path, in particular the same optical fibre which is used for spatial filtering, to transport the excitation signal and the fluorescence signal emitted in response, and using an optical system adapted to conjugate the focussing point in the tissue with said optical fibre.

The corresponding confocal imaging apparatus comprises the bundle of flexible optical fibres (usually called image guide) with, at its proximal end:

- the source emitting continuously or in pulsed mode at the excitation wavelength of one or more targeted fluorophores, typically a laser source;
- means for rapid scanning over time of the excitation beam produced by the source in lines and columns in a XY plane corresponding to the entry section of the image guide;
- means for injecting the excitation beam into one of the optical fibres;
- means for detecting the fluorescence signal; and
- control means, in particular for the scanning means.

Means are also provided adapted for the realization and the display of an image from the signals successively detected on each fibre.

At the distal end of the image guide in an optical head, intended to be brought into contact with the observed tissue, allowing the excitation beam to be focused at a given depth (tens of μm) and thus the realization of a subsurface image.

In practice, this type of apparatus has the following advantages in particular:

- on the distal side of the image guide there is only one focusing optic, which is less fragile and less costly than an optical head with incorporated scanning means, the replacement of

the optical head being able to be envisaged independently of the scanning means; moreover the head can be miniaturized, which is advantageous in endoscopy and also, in a general way, for increasing the precision of positioning;

an image guide made of flexible optical fibres, serves as an access arm to the site to be observed, which is important for an *in situ* application.--

Please replace the paragraph beginning at page 5, lines 11-20, with the following rewritten paragraph:

--The present invention proposes a solution for realizing an ~~in vivo in situ~~ *in vivo* and *in situ* image in real time, whether for a method with or without focusing on the exit of the fibre. The invention is based on respecting the sampling of the fibres (according to Shannon's criterion) which makes it possible to obtain an image reconstructed point by point which effectively corresponds to each fibre. This avoids loss of information when sampling all of the fibres one by one while still maintaining a minimum average number of images per second, i.e. in practice at least 12 images per second for a maximum mode of 640 x 640 pixels. The choice of detection frequency (pass-band of the detector) as a function of this minimum sampling then allows the detection, for each fibre, of the greatest possible number of fluorescence photons.--

On page 9, after line 10, please add the following
heading:

--BRIEF DESCRIPTION OF THE DRAWINGS--

On page 9, after line 19, please add the following
heading:

--DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS--